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54 **Pressure-sensitive adhesive having a broad spectrum anti-microbial therein.**

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## Description

This invention relates to a dermatologically acceptable composition made of a pressure-sensitive adhesive and a broad-spectrum antimicrobial agent uniformly dispersed therein which controllably releases from the composition when the composition is placed in contact with the skin.

Numerous pathogens are present on the human skin. In a hospital environment it is generally desired that the growth of disease-producing microorganisms be inhibited and preferably that these microorganisms be destroyed so as to control patient infection and encourage wound healing. As a result, the application to the skin surface of topical bactericidally active agents has become a standard part of the aseptic hospital technique.

The topical applications of broad-spectrum antimicrobials have been in the form of pre-operative skin preps, surgical scrub tissues, e.g. U.S. Patent 4,045,364, washes, wound cleaners, lotions and ointments. In some instances such a delivery is effective for the particular purpose for a limited period of time. Microorganisms that may have survived the initial application of the antimicrobial agent act as a seed causing the pathogen population in some instances to rise to their initial levels. Continuous application of an antimicrobial agent to the site is a means of inhibiting this increase in population.

While numerous biologically active agents have been incorporated into adhesive layers on a substrate to provide a continuous application to the body of the agent (FR 2,012,584), there has been no incorporation of a broad-spectrum antimicrobial into an adhesive layer which has been characterized by stability and unaltered activity of the broad-spectrum antimicrobial. Examples of various other agents that have been incorporated into adhesives are U.S. Patent 2,137,169 where phenol, thymol, menthol, etc. are added to a starch adhesive; U.S. Patent 3,249,109 where benzocaine was added to a tacky gelatin; U.S. Patent 3,632,740 where a corticosteroid is added to an adhesive; U.S. Patents, 3,734,097 where a microencapsulated antineoplastic agent is added to an adhesive (U.S. Patent 3,598,123 contains a similar disclosure); U.S. Patent 4,073,291 where Tretinoin is added to an adhesive; U.S. Patent 3,769,071 where 5-fluorouracil is incorporated into an adhesive; and U.S. Patent 3,896,789 where retinoic acid is incorporated into a pressure-sensitive adhesive tape. Previous attempts at incorporating a broad-spectrum antimicrobial into the adhesives have been frustrated by uncontrollable release which causes skin irritation in some patients and failure to obtain sufficient antimicrobial activity.

GB—A—1,297,280 discloses self-adhesive latex compositions for impregnating non-woven fabric to provide, for example, a tearable bandage or dressing material. The self-adhesive latex composition is substantially non-adhesive

towards uncoated portions of the non-woven fabric and may contain a germicide. The germicide may be dissolved in alcohol before being added to the aqueous latex composition if the germicide is water-insoluble.

The present invention is directed to a process for the formation of a storage stable pressure-sensitive adhesive composition and a composition which when placed in contact with skin uniformly and controllably releases the broad-spectrum antimicrobial agent with substantially unaltered activity. This is accomplished by the present invention with little or no skin irritation.

The term broad-spectrum is used herein to mean that the antimicrobial agent has activity against more than one type of microorganism, i.e. both gram positive and gram negative bacteria and would very likely also have activity against fungi and viruses (Reference: Federal Register, Vol. 39, No. 179).

The stable composition which results from the process of the present invention may be generally described as comprising a broad-spectrum antimicrobial agent and a dermatologically acceptable normally room temperature tacky pressure-sensitive adhesive (PSA) which is compatible with the antimicrobial agent. The PSA has an antiseptically active amount of the broad-spectrum antimicrobial agent homogeneously dispersed therein. By "homogeneously" it is meant that the broad-spectrum antimicrobial is distributed throughout the PSA, e.g. in uniform structure or composition, substantially in the manner that cream is dispersed in homogenized milk. This homogenous dispersion in the present invention allows for continuous, uniform and controlled release of the antimicrobial when the composition is in contact with the skin.

The process of the present invention involves forming an emulsifiable concentrate or an organic solution concentrate of the broad-spectrum antimicrobial and mixing it into the adhesive such that the broad-spectrum antimicrobial is homogeneously dispersed as a separate phase throughout the adhesive medium.

Stated another way, the process of the present invention involves the formation of a broad-spectrum antimicrobial solution comprising a broad-spectrum antimicrobial agent and a solvent and of a normally room temperature tacky pressure-sensitive adhesive which is compatible with the previously selected broad-spectrum antimicrobial agent. The broad-spectrum antimicrobial solution and pressure-sensitive adhesive are then mixed so that the solution containing broad-spectrum antimicrobial agent is homogeneously dispersed in the pressure-sensitive adhesive. The homogeneous dispersion is then spread or coated to a substantially uniform layer. This wet layer is then dried in order to remove the solvents. The resulting composition is comprised of an antiseptically active amount of the broad-spectrum antimicrobial agent homogeneously and stably dispersed in the pressure-sensitive adhesive.

The antimicrobial solution is comprised basically of a broad-spectrum antimicrobial agent and a solvent. As stated above the term broad-spectrum is used herein to mean that the antimicrobial agent has activity against both gram positive and gram negative bacteria and would very likely also have activity against fungi and viruses. Examples of antimicrobial agents which exhibit this broad-spectrum activity are iodine, chlorhexidine and polyvinylpyrrolidoneiodine (PVP-I), disclosed in U.S. Patent 4,128,633. The latter two broad-spectrum antimicrobial agents will be utilized herein to exemplify various aspects of the present process.

The antimicrobial agent solution is formed so as to contain approximately 1—50% by weight of a broad-spectrum antimicrobial agent and from approximately 99—50% by weight of a solvent. The final percentage selected is largely dependent on the solubility of the broad-spectrum antimicrobial agent utilized. For example, when polyvinylpyrrolidone (PVP-I) is utilized as the antimicrobial agent the solution preferably contains 35—40% by weight PVP-I and 65—60% by weight solvent.

The solvents used in the antimicrobial solution may be a single type of solvent or a combination of solvents such as water or water soluble solvents, e.g., methanol, ethanol, ethyl acetate, tetrahydrofuran, etc. The preferred solvent for PVP-I is either water or ethanol.

When the aforementioned PVP-I broad spectrum antimicrobial solution is incorporated into the pressure-sensitive adhesive, discussed below, the resulting PVP-I concentration in the final composition normally varies from 2—35% by weight. The optimum concentration of PVP-I on a solids basis will be approximately 10% (yielding 1% iodine). The upper limit of the concentration of PVP-I is determined by the maximum amount that may be contained without deleteriously affecting the adhesive properties of the adhesive. When chlorhexidine is used as the antimicrobially active agent, the antimicrobial solution comprises approximately 20 weight percent chlorhexidine diacetate and 80 weight percent solvent. The preferred solvent with chlorhexidine is denatured ethanol. The resulting final composition is normally 3—10 wt. % solid chlorhexidine.

The adhesive matrix is formed of a normally room temperature tacky pressure-sensitive adhesive which is chemically compatible with the previously selected broad-spectrum antimicrobial agent utilized in the broad spectrum antimicrobial solution.

Although it is generally believed that an acid medium renders many broad-spectrum antimicrobial agents more stable, it has been found that an acid adhesive is physically incompatible with antimicrobial agents such as PVP-I. The ultimate homogeneous distribution of broad-spectrum antimicrobial agent cannot be achieved in an acid adhesive so as to obtain controlled release without substantially altering the activity

of the agent. Also when a broad-spectrum antimicrobial solution containing a broad-spectrum antimicrobial agent is mixed with a pressure-sensitive adhesive which is acidic in nature, a premature coagulation of the adhesive has been experienced. It therefore is preferred that broad-spectrum antimicrobial agents such as PVP-I or chlorhexidine be utilized with normally room temperature tacky adhesive mediums which are substantially free of acidic components to facilitate the homogeneous dispersion of the broad-spectrum antimicrobial without the negative alteration to the activity of the antimicrobial agent. By "substantially free of acidic components" it is meant that the pressure-sensitive adhesive be substantially free of substituent groups which exhibit acid functionality, e.g. acrylic acid groups etc. Classes of such room temperature tacky pressure-sensitive adhesives which are or can be rendered substantially free of acidic components include polyacrylates, polyolefins, silicone adhesives, polyvinyl ethers, polyesters, polyurethanes, etc. as well as selected copolymers thereof. The formulation of these adhesives are well known in the art, e.g. U.S. Patents RE 24906, 2,973,286, 3,307,544, 3,645,835, etc. The actual choice of the pressure-sensitive adhesive is largely dependent on the end use to which the artisan will apply the final composition and the broad-spectrum antimicrobial agent that is to be incorporated therein. It will be appreciated by one skilled in the art that the aforementioned adhesive components might also include various chemical modifiers so as to enable them to have the utility dictated by the situation, e.g. tackifiers, crosslinkers, stabilizers, initiators, etc.

If a solvent is needed for use with the pressure-sensitive adhesive, the solvent should be chosen to be compatible with the broad-spectrum antimicrobial solution, e.g. with acrylic adhesives and chlorhexidine, a polar solvent could be utilized. The solvent of the adhesive solution for use with PVP-I preferably should be capable of solubilizing the solvent of the antimicrobial solution while at the same time being a non-solvent for the broad-spectrum antimicrobial agent.

After formation, the broad-spectrum antimicrobial solution and the pressure-sensitive adhesive are mixed such that the broad-spectrum antimicrobial solution is homogeneously dispersed in the pressure-sensitive adhesive. The mixing is performed at room temperature and may be accomplished utilizing a spatula or when necessary any apparatus which results in a shearing type mixing action, e.g. a Dispersator® sold by Premier Mill Corp., Temple, PA. It is believed that this mixing results in the broad-spectrum antimicrobial solution forming either a stable water-in-oil emulsion or a dispersed microfine phase in the second solution. For example, when 22 parts by weight of the broad spectrum antimicrobial solution comprising a 35% by weight broad-spectrum antimicrobial agent such as PVP-I, in water containing a non-ionic surfactant (discussed below) is mixed with 78 parts by

weight of a 44% solid adhesive solution, a very stable water-in-oil emulsion is formed wherein the dispersed phase consists of stable discrete water droplets averaging about 10  $\mu\text{m}$  in diameter. Alternatively, when the antimicrobial solution comprised of a broad-spectrum antimicrobial agent as PVP-I in an organic solvent containing a surfactant is mixed with the adhesive, it is believed that the solvent of the adhesive extracts the solvent of the antimicrobial solution causing the broad-spectrum antimicrobial in the form of PVP-I to separate out as a distinct minute separate phase of PVP-I particles. The presence of the non-ionic surfactant stabilizes the discrete second phase of PVP-I as microfine particles homogeneously dispersed in the adhesive. In some instances, certain adhesives appear to function as the surfactant and stabilize the PVP-I dispersion.

The homogeneous dispersion from above may then be spread or coated by means known to the art onto various backings to form dressings, drapes, tapes, etc. The preferred backing material for use with the present invention is a polyethylene film. This coating can be done by forming a substantially uniform layer of the homogeneous dispersion onto a release liner which facilitates the composition's later attachment to other substrates. Alternatively, the uniform layer of the homogeneous dispersion may be formed directly on to a flexible substrate thus eliminating the need for the release liner. The uniform layer of the homogeneous dispersion is then dried resulting in a composition which contains an antiseptically active amount of the broad-spectrum antimicrobial agent homogeneously and stably dispersed in the pressure-sensitive adhesive and capable of releasing the same when brought in contact with skin. By "stably" it is meant that a composition coating of 0.71 g (11 grains) per 0.155  $\text{m}^2$  (24 sq. in.) on a polyethylene backing can be exposed to a temperature of 48.8°C (120°F) at a relative humidity of 9% for two (2) weeks or to a dose of 2.5 megarads of gamma irradiation without substantial alteration of the physical appearance or of the chemical activity as tested by the starch test. Alternatively, microbiological activity of the composition can be tested by Zone Inhibition Assay which is described in detail below.

The starch test is performed by preparing an indicator solution. A drop of the Paragon Indicator solution is placed on the adhesive surface. Formation of blue coloration in the drop indicates availability of iodine.

The indicator solution is prepared by dissolving 62.5 g of Paragon Iodine Titration Indicator (Eastern Chemical, Division of Guardian Chemical Corp., Hauppauge, NY) in 250 ml of distilled water with stirring.

As stated briefly above, a surfactant may comprise approximately 0—5% of the antimicrobial solution in order to stabilize the broad-

spectrum antimicrobial. The surfactants used in the antimicrobial solution may have a wide variety of structures and a wide variety of physical properties such as are characterized by the hydrophilelipophile balance (HLB). Non-ionic surfactants preferably have a HLB value from 4 to 14. Suitable non-ionic surfactants include: Triton® X—100 (sold by Rohm & Haas, Philadelphia, Pa.) which is an ethylene oxide adduct of octyl phenol. Another useful surfactant is sold as Pluronic brand surfactants by Wyandotte Chemical Company of Wyandotte, Mich., which are condensates of ethylene oxide with hydrophobic bases formed by condensing propylene oxide with propylene glycol.

The invention is further illustrated by the following nonlimiting examples:

#### Example 1

2-ethylhexylacrylate/N-vinylpyrrolidone adhesive (90/10 weight percent) was synthesized as follows:

86.4 g. ethyl acetate, 0.88 g. ethanol, 77.3 g. heptane, 11.0 g. N-vinylpyrrolidone, 99.0 g. 2-ethylhexyl acrylate, and 0.294 g. azobisisobutyronitrile were charged to a 473.2 ml (one pint) bottle. The bottle was flushed with a stream of nitrogen for 3—4 minutes, sealed, and tumbled in a water bath at 55°C for 20 hours. The (non-volatile) solids of the solution were 39.4%. The inherent viscosity, measured in ethyl acetate at 30°C with a #50 Cannon-Fenske viscometer, was 0.735.

Next, 24.6 g. of a stock solution of a 35 wt. % polyvinylpyrrolidone-iodine complex (PVP-I) water solution was placed into a 100 ml wide-mouth bottle, to which was then added 0.86 g. of an ethylene oxide adduct of octyl phenol sold by Rohm & Haas as Triton® X—100. This surfactant/PVP-I solution was added to a bottle containing 73.1 g. of the previously synthesized 2-ethylhexylacrylate/N-vinylpyrrolidone adhesive. The resulting composition was stirred with a spatula to obtain a uniform dispersion. A uniform coating was applied to a release liner using a 15.2 cm (6") knife coater. The coating was then dried in a 93.2°C (200°F) oven. The dried film was then laminated to a  $3.81 \times 10^{-2}$  mm (1—1/2 mil) corona and quaternary amine antistat treated polyethylene film.

#### Example 2

6.6 g. of a 45% PVP-I ethanol solution was added to a bottle containing 26.0 g. of the 2-ethylhexylacrylate/N-vinylpyrrolidone adhesive from Example 1. This formulation was stirred with a microspatula to obtain a uniform dispersion. The coating/laminating procedure was the same as in Example 1. In Examples 1 and 2 small amounts of polyvinylpyrrolidone may be incorporated into the adhesive either as a physical mix or as an integral part of the adhesive so as to increase the compatibility of the PVP-I with the adhesive.

### Example 3

Preparation of an antimicrobial adhesive with Monsanto Gelva\* adhesives:

First a 80/20 blend of Monsanto Gelva\* adhesives containing 133.3 g. of 30- solids Gelva RA 737\* having a  $\bar{M}_n$  of 70,800 and  $\bar{M}_w$  of 722,900 and 22.7 g. of 44% solids Gelva RA 788\* having a  $\bar{M}_n$  of 77,350 and a  $\bar{M}_w$  of 493,000 was prepared. The 80/20 Gelva\* blend 37.5 g. was placed in a bottle containing 6.6 g. of 14.5% by weight PVP-I in EtOH. The formulation was stirred with a microspatula to obtain a uniform dispersion. The coating/laminating procedure was the same as Example 1.

\*Trademark

### Example 4

The biological activity of Example 1, 2 and 3 was determined by a Zone of Inhibition test utilizing the following procedure: The assay bacterium *Bacillus subtilis* was grown in rotary shake culture (200 rpm) for approximately 6 hours at 37°C. The growth medium, L-broth, consisted of the following ingredients dissolved in 1 l of distilled water and adjusted to pH 7.0: tryptone 10 g, yeast extract 5 g sodium chloride 10 g, glucose 1 g. This culture was diluted in sterile L-broth to 50% T@ 660 mu, further diluted 1:10, and inoculated at a ratio of 1:100 into molten soybean-casein digest agar medium (Inolex) maintained at 45—50°C. Assay plates were prepared by first pipesetting a 5 ml base layer of soybean-casein digest agar medium (TSA), allowing this to harden at room temperature in disposable petri dishes, and then overlaying with 5 ml of seeded TSA. These preparations were used the same day. The previously coated polyethylene films from Example 1, 2 and 3 were tested in the same way regardless of the antimicrobial incorporated into the adhesive layer. Ten 6 mm discs were cut from an evenly coated area (ie no visible flaws) with a heavy duty paper punch (Master Products, Series 25). The paper backing was removed from the coated disc with the aid of forceps and microspatula. The coated disc was then placed adhesive-side down on the seeded-agar surface, 4 per plate.

Reference discs were prepared differently depending on the antimicrobial agent. Aqueous solutions of chlorhexidine acetate ranging from

0.01 percent to 0.25 percent (w/v) were used to prepare discs containing 1 ug to 25 ug each from 10 ul aliquots applied to 6 mm filter paper discs (S and S No. 740-E).

Iodine reference disc were then prepared. A solution containing 10 percent iodine was prepared by dissolving 1 g of iodine and 1 g of sodium iodide in 10 percent aqueous acetone using a 10 ml volumetric flask. This stock solution, freshly prepared, and the same solvent were used to prepare 0.25, 0.5, 0.75, and 1.0 percent iodine solutions. From these dilutions, 10 ul aliquots were applied to 6 mm polyester fabric discs placed on the seeded agar surface to provide discs containing 25, 50, 75, 100 ug iodine each. (The polyester fabric was leached overnight in solvent to remove inherent antibacterial activity prior to punching). Each reference disc was covered with 2.54 cm (1 inch) square of 2-ml polyethylene to prevent vaporization prior to diffusion through the underlying agar.

The coated discs and reference disc assay plates were incubated overnight at room temperature. Zones of inhibition around the discs were measured to the nearest 0.5 mm with the aid of a binocular stereoscopic microscope. In the case of iodine antimicrobials, the coated discs were also removed to examine plates for areas of growth inhibition under the discs.

Assay results for reference antimicrobials using the preceding methods demonstrate that the diameter of the zone of inhibition measured in mm is linearly proportional to  $\text{LOG}_{10}$  concentration for each agent over the range examined. The release of antimicrobial from the adhesive of the present invention can be estimated by graphic interpolation of the inhibition values.

The biological activity (from zone of inhibition) for antimicrobial adhesives of Examples 1, 2 and 3 were all positive (19—30 micrograms of iodine per 6 mm disc) which is 90—100% of the total iodine charged.

*In vivo* efficacy on seeded human skin is exhibited by a 4—5 log reduction of *Staphylococcus aureus* and *Pseudomonas aeruginosa* after one hour.

### Example 5

A formulation was prepared as follows:

Gelva adhesive RA-737 (about 30% solids having a $\bar{M}_n$ of about 70,800 and a $\bar{M}_w$ of about 722,900)	480 g.
Gelva adhesive RA-788 (about 40% solids having a $\bar{M}_n$ of about 77,350 and a $\bar{M}_w$ of about 493,000)	90 g.
A solution containing 20 wt% chlorhexidine acetate (Imperial Chemical Industries, Ltd.) in denatured ethanol	27 g.
Additional denatured ethanol solvents	50 g.

The formulation was stirred at room temperature to yield a uniform solution of 3 wt% chlorhexidine acetate on adhesive solids. This solution

was coated on silicone release liner and dried to form a clear homogeneous adhesive film of coating weight equal to 11 grains/24 sq. in. The

adhesive film was laminated to a backing of a corona and quaternary amine antistat treated polyethylene film to form a composite construction containing the antimicrobial chlorhexidine acetate. The composite construction exhibited *in vivo* efficacy on seeded human skin of a one log reduction of *Staphylococcus aureus* and of *Pseudomonas aeruginosa* after one hour. No skin irritation was observed from the use of this composition.

#### Claims

1. A composition which releases an antiseptically active, broad-spectrum antimicrobial agent when placed in contact with skin, comprising an antiseptically active amount of a broad-spectrum antimicrobial agent and a dermatologically acceptable room temperature tacky pressure-sensitive adhesive which is chemically compatible with said broad-spectrum antimicrobial, said composition being characterized in that said broad-spectrum antimicrobial agent is stably dispersed in said pressure-sensitive adhesive homogeneously.

2. A composition according to claim 1 characterized in that said broad-spectrum antimicrobial agent is polyvinylpyrrolidone iodine complex or chlorhexidine.

3. A flexible backing material having attached thereto a composition according to claim 1 or 2.

4. A process for making a dermatologically acceptable composition according to claim 1, said process being characterized by the steps comprising forming a solution of a broad-spectrum antimicrobial agent; forming a room temperature, tacky, pressure-sensitive adhesive which is compatible with said broad-spectrum antimicrobial agent; mixing said antimicrobial agent solution and said pressure-sensitive adhesive such that the broad-spectrum antimicrobial agent from said antimicrobial agent solution is homogeneously dispersed in said pressure-sensitive adhesive; and drying said homogeneous dispersion so as to remove said solvents leaving an antiseptically active amount of said broad-spectrum antimicrobial agent homogeneously and stably dispersed in said pressure-sensitive adhesive.

5. The process of claim 4 characterized by the additional step of introducing a surfactant into said antimicrobial agent solution prior to mixing with said pressure-sensitive adhesive.

#### Patentansprüche

1. Zusammensetzung, die in Berührung mit der Haut ein antiseptisch wirksames, in einem breitem Spektrum antimikrobielles Mittel abgibt, mit einer antiseptisch wirksamen Menge eines in einem breiten Spektrum antimikrobiellen Mittels und einem bei einer hautverträglichen Zimmertemperatur klebfähigen Haftklebers, der mit dem in einem breiten Spektrum antimikrobiellen Mittel

chemisch verträglich ist, dadurch gekennzeichnet, daß das in einem breiten Spektrum antimikrobielle Mittel in dem Haftkleber homogen und stabil verteilt ist.

2. Zusammensetzung nach Anspruch 1, dadurch gekennzeichnet, daß das in einem breiten Spektrum antimikrobielle Mittel ein Polyvinylpyrrolidonjod-Komplex oder Chlorhexidin ist.

3. Flexibler Träger, an dem eine Zusammensetzung nach Anspruch 1 oder 2 angebracht ist.

4. Verfahren zum Erzeugen einer hautverträglichen Zusammensetzung nach Anspruch 1, dadurch gekennzeichnet, daß eine Lösung eines in einem breiten Spektrum antimikrobiellen Mittels hergestellt wird, daß ein bei Zimmertemperatur klebfähiger Haftkleber hergestellt wird, der mit dem in einem breiten Spektrum antimikrobiellen Mittel verträglich ist, daß die Lösung des antimikrobiellen Mittels und der Haftkleber derart miteinander vermischt werden, daß das in einem breiten Spektrum antimikrobielle Mittel aus der Lösung desselben in dem Haftkleber homogen dispergiert wird, und daß durch Trocknen der homogenen Dispersion Lösungsmittel entfernt werden, wobei eine antiseptisch wirksame Menge des in einem breiten Spektrum antimikrobiellen Mittels zurückbleibt, das in dem Haftkleber homogen und stabil verteilt ist.

5. Verfahren nach Anspruch 4, dadurch gekennzeichnet, daß die Lösung des antimikrobiellen Mittels vor deren Vermischen mit dem Haftkleber ein Tensid eingeführt wird.

#### Revendications

1. Composition qui libère un agent antimicrobien à large spectre, doué d'activité antiseptique, lorsqu'elle est mise au contact de la peau, comprenant une quantité à activité antiseptique d'un agent antimicrobien à large spectre et d'un adhésif sensible à la pression collant à la température ambiante, acceptable en dermatologie, qui est chimiquement compatible avec ledit agent antimicrobien à large spectre, ladite composition étant caractérisée en ce que l'agent antimicrobien à large spectre est dispersé de façon stable et homogène dans ledit adhésif sensible à la pression.

2. Composition suivant la revendication 1, caractérisée en ce que l'agent antimicrobien à large spectre est un complexe d'iode et de polyvinylpyrrolidone ou la chlorhexidine.

3. Support flexible portant une composition suivant la revendication 1 ou 2.

4. Procédé de préparation d'une composition acceptable en dermatologie suivant la revendication 1, ledit procédé étant caractérisé par les étapes qui consistent à former une solution d'un agent antimicrobien à large spectre; à former un adhésif sensible à la pression collant à la température ambiante, qui est compatible avec ledit agent antimicrobien à large spectre; à mélanger la solution d'agent antimicrobien et l'adhésif sensible à la pression de manière que

l'agent anti-microbien à large spectre provenant de la solution d'agent antimicrobien soit dispersé de façon homogène dans ledit adhésif sensible à la pression; et à sécher ladite dispersion homogène de manière à éliminer les solvants en laissant une quantité à activité antiseptique de l'agent antimicrobien à large spectre dispersée de

façon homogène et stable dans l'adhésif sensible à la pression.

5 5. Procédé suivant la revendication 4, caractérisé par l'étape supplémentaire d'introduction d'un surfactant dans la solution d'agent antimicrobien avant le mélange avec ledit adhésif sensible à la pression.

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